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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,365	02/13/2002	Yechezkel Barenholz	BARENHOLTZ=1A	5480

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/073,365	Barenholz
	Examiner	Art Unit
	Gollamudi Kishore	1615

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-49 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some* c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
- 4) Interview Summary (PTO-413) Paper No(s). _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

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DETAILED ACTION

The change of attorney dated 7-24-03 is acknowledged.

Claims included in the prosecution are 1-49.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 8-10, 20-30, 47 and 49 are rejected under 35 U.S.C. 112, second paragraph,

as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what applicant intends to convey by 'phospholipids are derived from soy oil' as recited in claims 8 and 22; soy oil is a triglyceride of fatty acids.

The examiner suggests reciting the chemical names for E-100, S-20 and others recited in claims 9, 10, 23, 24 and 47.

(ii) in claim 20 recites "adding to the solute obtained in step (a); first of all, there is no step (a) in (I); secondly according to step (I), the liposome-forming lipids are in a solution form in the organic solvent and there is no solute as such.

A claim should be complete in itself; claim 49 which recites 'an anti-oxidant formulation substantially as described in the specification' thus, is vague and indefinite.

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Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-5, 7-15, 17-24, 26, 28-33, 35-44, 46-47 and 49 are rejected under 35

U.S.C. 102(b) as being anticipated by Meybeck (5,034,228) of record.

Meybeck discloses topical liposomal formulations containing beta-carotene for dermatological and cosmetic applications. The applications include 'to fight aging' and protection against sun (protection against free-radicals, singlet oxygen). The compositions can also be administered orally. The method of preparation of liposomes disclosed by Meybeck appears to be the same as the instant method. The method involves dissolving the phospholipid and the carotenoid in an organic solvent and removing the solvent to prepare a dry preparation (instant method steps () and (ii), hydrating the powder with an aqueous medium and lyophilizing the liposomes and hydrating them again when needed. Although there is no explicit teaching in Meybeck that the liposome forming lipids in the organic solvent is to a level close to saturation, the amounts of the phospholipid used by Meybeck as seen from examples are more than the amounts noted in instant specification and therefore, deemed to be close to saturation . (abstract, col. 3, lines 19-46; Examples 1 and 17, and claims).

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5. Claims 1-5, 7-19, 31-44, 46-47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/13265 of record.

WO discloses liposomal formulations containing beta-carotene for prevention of oxidation damage caused by singlet oxygen and other reactive oxygen species. The liposomes are made from phospholipids including egg phosphatidylcholine. The mode of administration is either topical or oral (capsules or tablets) (abstract, pages 4-6, 9-11, Examples and claims).

6. Claims 1-19 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Stahl (FEBS Letters, 427, 1998).

Stahl discloses liposomal formulations containing carotenoid mixtures. The carotenoids include lycopene, lutein, beta-carotene. According to Stahl, mixtures of carotenoids are more effective than the single compounds (note the abstract, Materials and Methods and Tables). The intended use has no significance in composition claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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8. **Claims 20-26, 28-30 and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meybeck cited above.**

The teachings of Meybeck have been discussed above. In essence, Meybeck discloses topical liposomal formulations containing beta-carotene for dermatological and cosmetic applications. The applications include 'to fight aging' and protection against sun (protection against free-radicals, singlet oxygen). The compositions can also be administered orally (abstract, col. 3, lines 19-46; Examples 1 and 17, and claims). The method of preparation of liposomes disclosed by Meybeck is similar to instant method. The method involves dissolving the phospholipid and the carotenoid in an organic solvent and removing the solvent to prepare a dry preparation (instant method steps () and (ii), hydrating the powder with an aqueous medium and lyophilizing the liposomes and hydrating them again when needed. Although there is no explicit teaching in Meybeck that the liposome forming lipids in the organic solvent is to a level close to saturation, as pointed out above, the amounts of the phospholipid used by Meybeck as seen from examples are more than the amounts noted in instant specification. Assuming that they are different, it is deemed obvious to one of ordinary skill in the art to manipulate the amounts of the phospholipid since the phospholipid amounts determine how many liposomes are formed and how much of the lipophilic carotenoids are incorporated in the lipid bilayers. Meybeck does not teach cyclohexane as the organic solvent. However, the purpose the solvent is to dissolve the phospholipid, it is deemed obvious to one of ordinary skill in the art to select a

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suitable solvent as long as it serves the desired purpose. Meybeck does not teach a kit. However, it is deemed obvious to one of ordinary skill in the art to supply the components in the form of a kit so that the artisan can obtain fresh preparations of liposomes when needed.

9. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meybeck cited above, further in view of Mackaness (4,192,859).

The teachings of Meybeck have been discussed above. What is lacking in Meybeck is the use of cyclohexane as the solvent in the preparation of liposomes.

The use of cyclohexane would have been obvious to one of ordinary skill in the art, with the expectation of obtain at least similar results, since Mackaness teaches that organic solvents such as cyclohexane and chloroform could be used in dissolving the phospholipids in the preparation of liposomes (col. 3, lines 40-45).

10. Claims 1-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meybeck or WO 94/13265 cited above, further in view of Stahl cited above.

The teachings of Meybeck and WO 94 have been discussed above. What is lacking in these references are the teachings of the use of a combination of carotenoids or the use of lycopene.

Stahl as discussed above, discloses liposomal formulations containing carotenoid mixtures. The carotenoids include lycopene, lutein, beta-carotene. According to Stahl,

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lycopene is the most effective compound and the mixtures of carotenoids are more effective than the single compounds (note the abstract, Materials and Methods and Tables).

The use of lycopene as the carotenoid in Meybeck or WO would have been obvious to one of ordinary skill in the art since according to Stahl, lycopene is more effective than other carotenoids. The use of mixtures of carotenoids would have been obvious to one of ordinary skill in the art since Stahl teaches that mixtures of carotenoids are more effective than the single compounds.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *T.K. Page*, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

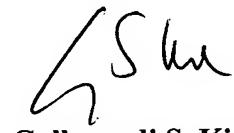
Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a

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properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.



Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

July 30, 2003